Veterinary Medicines Directorate

United Kingdom
Veterinary Medicines Directorate
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NATIONAL PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

MoxiSolv 18.92 mg/g Oral Gel for Horses and Ponies

Date Created: April 2023

MODULE 1

PRODUCT SUMMARY

Name, strength and pharmaceutical form	MoxiSolv 18.92 mg/g, Oral Gel for Horses and Ponies
Applicant	Bimeda Animal Health Limited 2/3/4 Airton Close Tallaght, Dublin 24 Ireland
Active substance	Moxidectin
ATC Vetcode	QP54AB02
Target species	Horses (including ponies)
Indication for use	Horses (including ponies): For treatment of infections caused by moxidectin sensitive strains of: **Large strongyles:** • *Strongylus vulgaris* (adults and arterial stages) • *Strongylus edentatus* (adults and visceral stages) • *Triodontophorus brevicauda* (adults) • *Triodontophorus serratus* (adults) • *Triodontophorus tenuicollis* (adults) **Small strongyles (adults and intraluminal larval stages):** • *Cyathostomum* spp. • *Cylicocyclus* spp. • *Cylicostephanus* spp. • *Cylicodontophorus* spp. • *Gyalocephalus* spp. **Ascarids:** • *Parascaris equorum (*adult and larval stages) **Other species:** • *Oxyuris equi* (adult and larval stages)

	• *Habronema muscae* (adults) • *Gasterophilus intestinalis* (L2, L3) • *Gasterophilus nasalis* (L2, L3) • *Strongyloides westeri* (adults) • *Trichostrongylus axei* The veterinary medicinal product has a persistent efficacy of two weeks against small strongyles. The excretion of small strongyles eggs is suppressed for 90 days. The veterinary medicinal product is effective against (developing) intramucosal L4 stages of small strongyles. At 8 weeks after treatment, early (hypobiotic) L3 stages of small strongyles are eliminated.

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Product Information Database of the Veterinary Medicines Directorate.

(www.gov.uk/check-animal-medicine-licensed)

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Generic application in accordance with Article 13(1) of Directive 2001/82/EC as amended.
Date of conclusion of the procedure	24/01/2023

I. SCIENTIFIC OVERVIEW

The quality / safety / efficacy aspects of this product are identical to Equest Gel Oral 18.92 mg/g, Oral Gel for Horses and Ponies. The initial application for Equest Gel Oral was assessed before there was a requirement to have a public assessment report, therefore no details in this section are available.

II. QUALITATIVE AND QUANTITATIVE PARTICULARS OF THE CONSTITUENTS

II.A. Composition

The product contains moxidectin and the excipients benzyl alcohol, poloxamer 407, propylene glycol, simethicone, polysorbate 80, sodium dihydrogen phosphate, disodium phosphate, disodium edetate and purified water.

The container/closure system consists of an HDPE syringe barrel and plunger assembly comprised of plunger, dose ring and seal with a LDPE cap/seal. The particulars of the containers and controls performed are provided and conform to the regulation.

The choice of the formulation and the presence of preservative are justified.

The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.

II.B. Description of the Manufacturing Method

The product is manufactured fully in accordance with the principles of good manufacturing practice from a licensed manufacturing site. The manufacturing method consists of mixing, heating and cooling.

Process validation data on the product have been presented in accordance with the relevant European guidelines.

II.C. Control of Starting Materials

The active substance is moxidectin, an established active substance described in the European Pharmacopoeia. The active substance is manufactured in accordance with the principles of good manufacturing practice.

The active substance specification is considered adequate to control the quality of the material. Batch analytical data demonstrating compliance with this specification have been provided.

All excipients comply with Ph. Eur.

II.C.4. Substances of Biological Origin

Scientific data and/or certificates of suitability issued by the EDQM have been provided and compliance with the Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products has been satisfactorily demonstrated.

II.D. Control Tests Carried Out at Intermediate Stages of the Manufacturing Process

Visual tests for clarity and absence of bubbles.

II.E. Control Tests on the Finished Product

The finished product specification controls the relevant parameters for the pharmaceutical form. The tests in the specification, and their limits, have been justified and are considered appropriate to adequately control the quality of the product. Satisfactory validation data for the analytical methods have been provided. Batch analytical data from the proposed production site have been provided demonstrating compliance with the specification. Control tests on the finished product are those for: appearance, pH, viscosity, moxidectin assay, moxidectin identification, moxidectin impurities, benzyl alcohol assay, benzyl alcohol identification, dissolution, content uniformity, and bioburden.

II.F. Stability

Stability data on the active substance have been provided in accordance with applicable European guidelines, demonstrating the stability of the active substance when stored under the approved conditions.

G. Other Information

Shelf-life of the veterinary medicinal product as packaged for sale: 2 years.
Shelf-life after first opening the immediate packaging: 6 months.
Do not store above 25°C.

III. SAFETY AND RESIDUES DOCUMENTATION (PHARMACO-TOXICOLOGICAL)

III.A Safety Documentation

Pharmacological Studies

Bibliographical data has been provided which show that moxidectin acts by interacts with GABA and glutamate gated chloride channels to induce an irreversible resting state. The applicant has also provided bibliographical data which show that moxidectin undergoes partial biotransformation by hydroxylation in the body.

Toxicological Studies

Not required due to the legal basis of the application.

User Safety

A user risk assessment was provided in compliance with the relevant guideline.

Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product. Therefore the following applicant's user recommendations are appropriate:

Avoid direct contact with skin and eyes.
The use of protective gloves is recommended. Wash hands or any exposed area after use.
Do not smoke, drink or eat while handling the veterinary medicinal product.
In the event of eye contact, flush the eye with copious amounts of clean water and seek medical advice.

Environmental Safety

The Environmental Risk Assessment (ERA) was carried out in accordance with VICH and CVMP guidelines.

Phase I:
The product is a parasiticide used in pasture animals and a Phase II ERA was required. (Question 16 VICH decision tree).

Phase II Tier A:
A Phase II tier A data set was provided according to the requirements of the VICH GL 38 and the CVMP guideline in support of the VICH guidelines including studies on physico-chemical properties, environmental fate and effects. Studies were carried out using the active substance moxidectin unless indicated otherwise.

Physico-chemical properties

Study type	Guideline	Result

Study type	Guideline	Result
Water solubility	OECD 105	0.47 mg/l (at 20°C ± 0.5°C)
Dissociation constants in water pKa	OECD 112	Could not be determined
UV-Visible Absorption Spectrum	OECD 101	n/a
Melting Point/Melting Range	OECD 102	324°C
Vapour Pressure	OECD 104	4.66E-20 (at 25 ºC)
n-Octanol/Water Partition Coefficient $logP_{ow}$	OECD 107	7.08

Environmental fate

Study type	Guideline	Result
Soil Adsorption/Desorption	OECD 106	mean K_{Foc}^{ads} 35406
Aerobic and Anaerobic Transformation in Soil	OECD 307	worst-case DT_{50} 78.65 d at 20ºC

Environmental effects

Study type	Guideline	Endpoint	Result
Algae, Growth Inhibition Test/*Species*	OECD 201	EC50	470 µg/l
Daphnia sp. immobilisation	OECD 202	EC50	0.958 µg/l
Fish, acute toxicity/*Species*	OECD 203	LC50	0.621 µg/l
Earthworm/*Species* subacute/reproduction	OECD 220/222	EC10	0.63 mg/kg
Dung fly larvae	OECD 228	EC50	3400 mg/kg fwt
Dung beetle larvae	OECD draft	EC50	70.4 µg/kg fwt

Exposure assessment (Predicted exposure concentration)

PEC value for soil, groundwater and surface water were calculated using the equations provided in the CVMP guidelines. The dose and duration of treatment were taken from the proposed SPC of the product. The following PEC values were calculated.

Target	PEC

Target animal	PEC			
	Soil (µg/kg)	Groundwater (µg/l)	Surfacewater (µg/l)	Dung µg/kg (fw)
Horse	0.96	0.0003	0.000097	2594 µg/kg (fw)

Risk Characterisation (Risk Quotient)
Using the assessment factors (AF) in VICH guidelines predicted no effect concentrations (PNEC) were calculated and compared with the PEC values for each target animal as follows.

Horses

Test organism	PNEC	PEC	RQ
Algae, Growth Inhibition	4.7 µg/	0.000097 µg/l	<0.01
Daphnia sp. immobilisation	0.000958 µg/l		0.10
Fish, acute toxicity	0.000621 µg/l		0.16
Earthworm reproduction	63 µg/kg	0.96 µg/kg	0.02
Dung fly larvae	0.70 µg/kg	2594 µg/kg (fw)	3705
Dung beetle larvae	34 µg/kg		76

As the RQ value for dung fauna were >1 further assessment of the environmental risk was required.

PEC Refinement & Tier B
As the octanal water partition co-efficient was >4, the applicant correctly considered bioaccumulation. Results from a proprietary OECD 305 study indicate that the substance is bioaccumulative (BCF_{KLG} = 4380 l/kg). Secondary poisoning was considered by the applicant and no risk to was indicated for fish and earthworm eating predators.

A risk was determined for dung flies, dung beetles, and earthworms from exposure to dung pats; and it has been agreed that environmental warnings and risk mitigation measures will be required to address this risk.

Concerning risk to for groundwater, the PEC for groundwater is less than the trigger value for assessment of 0.1 µg/l. Nevertheless, due to the high toxicity of the substance, a risk characterisation groundwater biota was carried out and no risk was indicated.

Regarding the PBT assessment, based on data provided in the dossier, the active substance is persistent, bioaccumulative and toxic. These findings are

not entirely in agreement with the outcome of a recent Article 35 referral conducted by the CVMP involving all VMPs containing moxidectin for food producing species, where it was concluded that moxidectin classifies as very persistent, bioaccumulative and toxic. Nevertheless, the substance still classifies as PBT and the warnings which were agreed during the 2017 Article 35 referral for moxidectin containing veterinary medicines used in cattle, sheep and horses still apply.

III.B.2 Residues documentation

Residue Studies

Not required due to the legal basis of the application.

MRLs

Moxidectin is listed in Annex 2 of Regulation 90/2377.

Pharmacologically active substance	Animal species	MRLs	Target Tissue
Moxidectin	Equidae	50 µg/kg 500 µg/kg 100 µg/kg 50 µg/kg	Muscle Fat Liver Kidney

Withdrawal Periods

Meat and offal: 32 days.
Not authorized with use in animals producing milk for human consumption.

IV. CLINICAL DOCUMENTATION

IV.I. Pre-Clinical Studies

Pharmacology

Not required due to the legal basis of this application.

Tolerance in the Target Species

Tolerance studies were not required because this is a generic application.

IV.II. Clinical Documentation

Not required due to the legal basis of this application.

V OVERALL CONCLUSION AND BENEFIT– RISK ASSESSMENT

The data submitted in the dossier demonstrate that the benefit/risk profile of the product is favourable.

MODULE 4

POST- AUTHORISATION ASSESSMENTS

The SPC and package leaflet may be updated to include new information on the quality, safety and efficacy of the veterinary medicinal product. The current SPC is available on the Product Information Database of the Veterinary Medicines Directorate website.

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The post-authorisation assessment (PAA) contains information on significant changes which have been made after the original procedure which are important for the quality, safety or efficacy of the product.

The PAA for this product is available on the Product Information Database of the Veterinary Medicines Directorate website.

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